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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/537,858	03/28/2000	Paul Proost	49674	5522

03/22/2002

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 03/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/537,858	Applicant(s) PROOST ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2002*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 March 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s).

4)☒ Other: Sequence Notice (copy).

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 1/15/02 (Paper No. 14), is acknowledged.
Claims 1-14 have been cancelled.
Claims 15-23 have been added and are pending.

Claims 15-23 *are under consideration in the instant application.*

2. This Office Action will be in response to applicant's arguments, filed 1/15/02 (Paper No. 14).
The rejections of record can be found in the previous Office Action (Paper No. 11).

It is noted that New Grounds of Rejection are set forth herein.

3. Applicant's cancellation of claims 1-4, 9 and 12 have obviated the previous objections and rejections with respect to these claims.

4. Sequence compliance: Applicant's provision of a CRF, Sequence Listing, and Statement that the contents are identical on 1/15/02 (Paper No. 14), is acknowledged. The CRF has been found acceptable and entered.

Applicant's provision of instant SEQ ID NO:2 (corresponding to the mature RANTES protein of 68 amino acids which begins with the sequence Ser-Pro-Tyr-Ser-Ser) has addressed the previous requirement for a definite numbering system for the truncated forms of RANTES.

However, the changes made in this bona fide attempt to respond to the Notice of Comply that accompanied Paper No. 11 have now resulted in the omission of the sequence found in Figure 1 from the sequence listing.

Therefore, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason set forth above and on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

In addition, Applicant is required to identify the nucleotide and amino acid sequences with SEQ. ID NOS wherever sequences occur in the specification and drawings in order to satisfy the requirements of 37 CFR 1.821 (d) (see also MPEP 2422.02-2422.03).

In particular, it is noted that the RANTES sequence presented in Figure 1 requires reference to the appropriate SEQ ID NO: (once provided), either in the Figure itself or in the Brief Description of the Drawings.

It is suggested that Applicant amend the sequence presented under instant "SEQ ID NO:1" to provide the [illegible] shown in Figure 1, and amend the "Brief Description of the Drawings" to indicate that the

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Application 97116863.8 filed in Europe on 9/29/97; application 97122471.2 filed in Europe on 12/19/97; and application 98104216.1 filed in Europe on 3/10/98 each appear to provide adequate written support for a truncated form of RANTES lacking residues 1 and 2 (that is, "RANTES (3-68)")and a mature RANTES protein comprising 68 amino acids ("RANTES (1-68)").

In addition, each of the priority documents appears to provide adequate written support for a RANTES protein missing "up to 5" amino terminal amino acids.

However, the phrase "up to 5" does not provide adequate written support for the instant language of "lacking NH_2-terminal amino acids corresponding to amino acid residues 1, 1-2, 1-3 or 1-4 of naturally-occurring RANTES (SEQ ID NO:2)". The instant claim language encompasses forms of RANTES that include NH_2-terminal truncations of greater than 5 amino acids. As noted previously in Paper No. 11 and again below, the instant claim language can be interpreted to be drawn to any protein lacking these residues, regardless of whether or not additional residues are also missing.

Thus the effective filing date of instant claims 15-16 and 18-23 is considered to be September 28, 1998, while instant claim 17 does appear to have an effective filing date of September 29, 1997.

6. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
It is noted that required drawing changes are no longer being held in abeyance by the Office.
Please see the form PTO-948 previously provided as part of Paper No. 11.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office

7. Claims 19 and 20 are objected to because of the following informalities: "lacksNH2-terminal" should read -- lacks NH_2-terminal -- as recited in claims 15-16 and 18. Appropriate correction is required.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 15-16 and 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 15-16 and 18-23 are ambiguous in the recitation of "lacking ....residues 1, 1-2, 1-3 or 1-4", "lacks... residues 1-2", "lacks... residue 1", "lacks... residues 1-3" and "lacks... residues 1-4".

As currently recited the meaning of these phrases is unclear. For example, the claims can be interpreted to be drawn to any protein lacking these residues, *regardless of whether or not additional residues are also missing*. Alternatively, the claims can be interpreted to be drawn to a protein lacking ONLY either residue 1, residues 1-2, etc.

Applicant's argument, filed 1/15/02, that the addition of a SEQ ID NO: obviated the rejection of record as it applies to the instant claims has been fully considered but has not been found persuasive essentially for the reasons of record in Paper No. 11.

Inclusion of a SEQ ID NO: by itself does not establish the metes and bounds of the instant claims when the ambiguity is associated with the number of amino acids lacking from the amino terminal.

B) Regarding claims 15-16 and 18-23, the phrase "naturally-occurring RANTES (SEQ ID NO:2)" renders the claim indefinite for at least two reasons.

As previously noted in Paper No. 11, the specification does not appear to provide a clear definition of the term "naturally-occurring RANTES". Further, the specification indicates on page 12 at lines 13-16 that the form of RANTES lacking residues 1 and 2 compared to "intact" RANTES are both naturally occurring forms. Therefore the term "naturally occurring" is ambiguous as currently recited.

In addition, although Applicant has argued in the amendment filed 1/15/02 that the rejection of record would not apply to the instant claims because of the inclusion of a sequence identifier; the placement of SEQ ID NO:2 within parenthesis fails to establish the metes and bounds of the instant claims because it is unclear whether the limitation of SEQ ID NO:2 included in the parenthesis is part of the claimed invention. See MPEP § 2173.05(d).

It is suggested that Applicant amend the claims to recite "naturally-occurring RANTES consisting of SEQ ID NO:2", or to simply refer to the sequence identifier.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. Claims 15-16, 18 and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Oravecz et al (J. Exp. Med. 1997;186:1865-1872, IDS AT; see entire document).

Applicant's arguments, filed 1/15/02, have been fully considered but have not been found convincing.

Applicant argues that the Oravecz et al. have a publication date that is after Applicant's priority date and is therefore not available as art.

However, for the reasons discussed supra with respect to the issue of the effective filing date of the claims, the priority date of claims 15-16 and 18-23 is considered to be September 28, 1998. Therefore Oravecz et al. is available as prior art with respect to these claims.

As previously noted, Oravecz et al. teach an amino-terminally truncated RANTES, lacking amino acids corresponding to amino acid residues 1-2 of the amino acids sequences of the naturally-occurring RANTES of SEQ ID NO:2 (see entire document, e.g., Abstract). Oravecz et al. also teach that RANTES lacking amino-terminal amino acids 1-2 is a potent antagonist of HIV-1 (e.g. bridging paragraph of pages 1869-1870, and Figure 7). In addition, although a pharmaceutical composition comprising a truncated RANTES in a pharmaceutically acceptable carrier is not explicitly taught, the formulation of the protein used in the cell culture experiment of Figure 7 is such a composition.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced protein. In addition, Applicant is reminded that intended uses do not carry patentable weight per se, and the claim reads on the active or essential ingredients.

The rejection is therefore maintained as it applies to the instant claims.

12. Claims 15-18 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Noso et al. (J. Immunol. 1996;156:1946-1953, of record, see entire document).

Applicant asserts that Noso et al. do not teach isolation of the amino-terminally truncated RANTES and further argues that Noso et al. do not teach that the truncated RANTES has chemokine antagonistic activity.

As previously noted, Noso et al. teach an amino-terminally truncated RANTES consisting of 66 amino acids and derived from dermal fibroblasts (see entire document; e.g. page 1948 2nd column, especially 5th paragraph, and Figure 3). The amino acid sequence of SEQ ID NO:3 would be an inherent property of the RANTES taught by Noso et al. since Figure 3 indicates that it is the amino acids corresponding to positions 1 and 2 that are missing from the 68 amino acid from of RANTES. Further, the RANTES taught by Noso et al. is a naturally-occurring RANTES lacking amino acids 1-2 of SEQ ID NO:2. In addition, Noso et al. teach glycosylated species of this truncated form of RANTES (e.g. page 1948, 2nd column, especially 5th paragraph).

Contrary to Applicant's assertions, Noso et al. do teach isolation of RANTES lacking amino acids 1 (Ser) and 2 (Pro), which is inherently a form of RANTES that has the amino acid sequence of SEQ ID NO:3 (or SEQ ID NO:2 lacking residues 1-2) (see page 1950, especially Figure 3).

Applicant is again reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced protein since they do not appear to differ in structure versus the RANTES (3-68) protein characterized by Applicant.

The rejection is therefore maintained as it applies to the instant claims.

13. Claims 15-16, 18-20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Gong et al. (J. Biol. Chem. 1996;271:10521-10527, IDS AO; see entire document).

Applicant's arguments, filed 1/15/02, have been fully considered but have not been found convincing.

Applicant asserts that Gong et al. provides no disclosure of any antagonistic activity of a truncated material as disclosed in the present application.

As previously noted, Gong et al. teach amino-terminally truncated RANTES lacking NH_2-terminal amino acids corresponding to amino acid residues 1, 1-2, 1-3, or 1-4; and having chemokine antagonistic activity (see entire document, especially Figure 1 and Table I).

Thus contrary to Applicant's assertions, Gong et al. do teach that the truncated RANTES is antagonistic.

As also noted previously, the instant claims are not limited to truncations involving ONLY amino acids 1 or 1-2, 1-3 or 1-4. In addition, although truncated RANTES in a pharmaceutically acceptable carrier is not explicitly taught, such a carrier is inherently present in the formulations of the protein used in the cell culture experiments of Figures 2-4.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced protein. In addition, Applicant is reminded that intended uses do not carry patentable weight per se, and the claim

14. Claims 15-16 and 18-23 are rejected under 35 U.S.C. 102(e) as being anticipated by Rollins et al. (US Pat. No. 5,739,103, of record, see entire document).

Applicant's arguments, filed 1/15/02, have been fully considered but have not been found convincing.

Applicant argues that Rollins et al. is directed to truncations of MCP-1, and not RANTES, because all of the Examples and the trust of the discussion of Rollin et al. is limited to MCP-1.

However, as previously noted Rollins et al. teach and claim amino-terminally truncated chemokines having antagonistic activity, including RANTES; and methods comprising administering amino-terminally truncated chemokines including RANTES (see entire document, especially columns 3 and 6-8 as well as the claims). The amino-terminally truncated RANTES taught by Rollins et al. include truncation of at least amino acids 1 and 2, since column 3 (as well as claims 5-7) teach that the truncation is to be "about 1 to about 10 or about 2 to about 7". It is noted that the instant claims are not limited to truncations involving ONLY amino acids 1 or 1-2, 1-3 or 1-4.

In addition, Rollins et al. teach recombinant production of amino-terminally truncated chemokines in eukaryotic cells, which would inherently result in a glycosylated protein (e.g., column 8, especially lines 11-20). Finally, Rollins et al. teach the formulation of the amino-terminally truncated RANTES in a pharmaceutically acceptable carrier for administration to a patient for treatment of a RANTES-mediated disease (e.g. columns 6-7); thus the limitation of a pharmaceutical composition comprising amino-terminally truncated RANTES is met.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations, such as the amino acid sequence of RANTES, would be inherent properties of the referenced protein.

The rejection is therefore maintained as it applies to the instant claims.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35

16. Claims 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gong et al. (J. Biol. Chem. 1996;271:10521-10527, IDS AO).

Applicant's arguments, filed 1/15/02, have been fully considered but have not been found convincing.

Applicant asserts that Gong et al. provides no disclosure of any antagonistic activity of a truncated material as disclosed in the present application.

The claims are drawn to amino-terminally truncated RANTES, lacking NH2-terminal amino acids corresponding to amino acid residues 1, 1-2, 1-3, or 1-4 and having antagonistic activity, and a pharmaceutical composition thereof.

Gong et al. have been discussed supra, as have been Applicant's arguments with respect to Gong et al. As discussed supra and previously, Gong et al. teach amino-terminally truncated RANTES lacking amino acids 1, 1-2, 1-3, and 1-4; and having antagonistic activity.

Gong et al. differ by not teaching an amino-terminally truncated RANTES having the amino acid sequence of SEQ ID NO:3 and by not explicitly teaching a pharmaceutical composition comprising the amino-terminally truncated RANTES.

However, Gong et al. also teach that the functional activity of RANTES is encoded in amino acids 1-5, since various truncations which included amino acids 1-5 resulted in forms of RANTES that lacked functional activity (e.g., page 10523, "Functional Activity of Shortened Analogs"). In addition, Gong et al. teach that truncations of RANTES involving amino acid residues 1-7, 1-8, 1-9 and 1-10 results in binding by these truncated forms of RANTES to receptors not normally bound by full length RANTES (e.g., page bridging paragraph of pages 10524 and 10525), causing Gong et al. to conclude that the specificity of RANTES lay within residues 1-6 (e.g., page 10525 last paragraph). Gong et al. teach screening of the various truncation in several assays which permit determination of whether a truncated form of RANTES is an antagonist, and how efficiently that particular truncation functions as an antagonist relative to other RANTES truncations (see entire document, especially the assays discussed in the Results section). Finally, Gong et al. teach that chemokine antagonists can be used to block the infiltration of cells during inflammation (e.g., see Discussion on page 10526-10527).

Therefore, the ordinary artisan at the time the invention was made would have been motivated to provide additional truncations of RANTES, including SEQ ID NO:3, by focusing on residues 1-6 of the amino terminal in order to identify truncated forms of RANTES that were antagonistic for RANTES, but that did not cross inhibit interactions of other chemokines with their receptors. Given the teachings of Gong et al. that functional activity requires residues 1-5, the ordinary artisan would have been further motivated to produce and screen truncations of RANTES lacking amino terminal residues 1, 1-2, 1-3, and 1-4. In addition, given the teachings of Gong et al. that multiple amino terminal truncations of RANTES result in forms of RANTES having chemokine antagonistic activity and the teachings of assays for assessing antagonistic activity; the ordinary artisan at the time the invention was made would have had a reasonable expectation of success in producing the claimed invention, including SEQ ID NO:3, as a matter of routine optimization.

Further, the ordinary artisan would have been motivated to provide pharmaceutical compositions comprising any such antagonists in order to evaluate their relative efficacy in various disease models of inflammation, as taught by Gong et al.; and would have had a reasonable expectation of successfully utilizing these RANTES antagonistic pharmaceutical compositions in inhibiting at least some models of [illegible] amino terminally truncated RANTES antagonistic

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection is maintained as it applies to the instant claims.

17. No claim is allowed.

18. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner

PHILIP GAMBEL PH.D.

Notice to Comply	Application No.	Applicant(s)	
	09/537,858	PROOST ET AL.	
	Examiner	Art Unit	
	Jessica H. Roark	1644	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2 This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3 A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4 A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7 Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
Technical Assistance.....703-287-0200
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